REMARKS

Claims 51-56 are pending in the subject application. By this Amendment, applicants have amended claims 51-56 and added new claims 57 and 58.

The amendments to claims 51 and 55 are fully supported in the specification, *inter alia*, as follows: Claim 51: page 2, lines 12-16; page 4, lines 10-17; page 11, lines 10-13 and 32-34; page 12, lines 10-13; page 14, lines 1-3; page 19, lines 3-4; page 36, lines 12-16; and Claim 55: page 11, lines 27-29; page 26, line 2 of Table 1 legend; and page 33, lines 5-6. Thus, applicants maintain that these amendments do not raise any issue of new matter. Similarly, no new matter is introduced by amendments to claims 52-54 and 56 which merely involve deleting the recitation of a "portion of an antibody", and in the case of claim 52, rewriting the claim in dependent format.

New claims 57 and 58 are also fully supported in the specification as filed, and thus do not raise any issue of new matter. Specifically, support for these new claims may be found in the specification, *inter alia*, at page 4, lines 26-30 and 10-13; page 12, lines 10-13; and page 22, lines 27-30. Accordingly, applicants respectfully request that the Examiner enter this Amendment. Upon entry of this Amendment, claims 51-58 will be pending and under examination.

The Claimed Invention

This invention provides an isolated antibody capable of binding to a human chemokine receptor, preferably a CCR5 receptor, on the surface of a CD4+ cell and inhibiting HIV-1 infection of such CD4+ cell. The invention further provides a pharmaceutical composition comprising the instant antibody and a

pharmaceutically acceptable carrier, wherein, in a preferred embodiment, the antibody is present in an amount effective to inhibit HIV-1 infection.

Rejections under 35 U.S.C. §101

The Examiner rejected claims 51-56 under 35 U.S.C. §101 because the claimed invention is allegedly directed to non-statutory subject matter. The Examiner stated that the invention is directed to "an antibody or a portion of an antibody" capable of binding a chemokine receptor. The Examiner further stated that an antibody, or a portion of an antibody such as an amino acid, is a product of nature. The Examiner also stated that, accordingly, claims 51-56 are directed to non-statutory subject matter. The Examiner advised that amending the claims to recite "[a] purified antibody or a purified portion of an antibody" would overcome this rejection.

In response and without conceding the correctness of the Examiner's position, applicants note that the sole independent claim, claim 51, as amended, is directed to an *isolated* antibody. Applicants maintain that since an isolated antibody is not a product of nature, the instant claims, as amended, are not directed to non-statutory subject matter.

Rejections under 35 U.S.C. §102

The Examiner rejected claims 51 and 52-55 under 35 U.S.C. §102(b) as allegedly anticipated by "Hirata" (Hirata, Y. et al. [1989] Characterization of IL-6 Receptor Expression by Monoclonal and Polyclonal Antibodies, J.Immunol. 143: 2900-2906).

Specifically, the Examiner stated that, regarding claim 51, Hirata teaches an antibody or a portion of an antibody capable

of binding to a chemokine receptor on the surface of a CD4+ cell (citing pages 2901 and 2905).

The Examiner also stated that, regarding claim 51 [*sic* claim 52], Hirata teaches an antibody or a portion of an antibody capable of binding to a CCR5 chemokine receptor on the surface of a CD4+ cell (*Id.*).

The Examiner further stated that, regarding claim 53, Hirata teaches the antibody or a portion of an antibody of claim 51 or 52, wherein the CD4+ cells is a PM-1 cell (*Id.*).

The Examiner additionally stated that, regarding claim 54, Hirata teaches the antibody or a portion of an antibody of claim 51 or 52, wherein the CD4+ cell is a primary CD4+ T-cell (*Id.*).

Regarding claim 55, the Examiner also stated that Hirata teaches the antibody or a portion of an antibody of claim 51 or 52, wherein the CD4+ cell is a PMBC cell (*Id.*).

In response, applicants respectfully traverse the rejection of claims 51-55 as anticipated by Hirata. With respect to claim 51, applicants note that Hirata discloses antibodies to the interleukin-6 receptor (IL-6R). Applicants respectfully point out to the Examiner that IL-6R is a cytokine receptor whereas the instant claims are directed to an antibody which is specific to a chemokine receptor. Applicants note that although chemokines constitute a subset of cytokines, chemokine receptors are structurally distinct from cytokine receptors. For the Examiner's convenience, applicants attach hereto as **Exhibit A** definitions of chemokines and cytokines (including the IL-6 family) and their respective receptors obtained from *The Dictionary of Cell and Molecular Biology* (Third edition, J.M. Lackie and J.A.T. Dow [1999] Academic Press, London; available

online at http://www.mblab.gla.ac.uk/~julian/Dict.html).

Applicants note that, as disclosed in the subject specification at page 25, lines 8-9 and as expanded upon by Lackie and Dow (1999), chemokine receptors are G-protein-linked serpentine receptors, i.e., they have seven membrane-spanning domains and are coupled to heterotrimeric G-proteins. By contrast, cytokine receptors share a common gp130 subunit but are not serpentine receptors. Thus, antibodies such as those disclosed by Hirata that bind to IL-6R, a cytokine receptor, are unrelated to an antibody capable of binding to an anti-chemokine receptor such as is claimed in the subject invention. Applicants maintain, therefore, that claim 51 is not anticipated by Hirata.

Regarding claim 52, applicants note that CCR5 is a specific example of a chemokine receptor. As discussed above, Hirata discloses antibodies that bind the cytokine receptor, IL-6R, and not the CCR5 receptor or any chemokine receptor. Thus, applicants maintain that claim 52 is not anticipated by Hirata.

With respect to claims 53-55, applicants maintain that, as discussed above, Hirata does not teach the antibody of claim 51 or 52, and thus does not anticipate claims 53-55 which depend from claim 51 or 52. Moreover, applicants note that the "PM-1" cell disclosed by Hirata is a hybridoma which produces anti-IL-6R antibodies (see Hirata, page 2901, first paragraph of *Results*), whereas the PM-1 cell taught in the subject specification is a T cell (see specification at, *inter alia*, page 25, lines 19-22; page 26, first line of Table 1 legend; Lusso et al. (1995) attached hereto as **Exhibit B**, page 3713, first paragraph of *Materials and Methods*). Thus, applicants maintain that the Examiner's rejection of claims 53-55 as anticipated by Hirata is without merit on the additional ground that the PM-1 cell taught by Hirata is unrelated to the PM-1 cell disclosed in the subject

application which is a CD4+ t cell.

Rejections under 35 U.S.C. §112, First Paragraph

Enablement

The Examiner rejected claims 51-56 under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

The Examiner stated that the determination of whether experimentation is "undue" weighs a number of factors. The Examiner further stated that these factors include the breadth of the claims, the state of the prior art, the level of predictability in the art, the existence of working examples, and the quantity of experimentation that is needed to make and use the invention based on the content of the disclosure (citing *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404).

The Examiner stated that in the present case, applicant's invention is broadly drawn to an antibody, or a portion of an antibody, that is capable of binding to the CCR5 receptor. The Examiner also stated that, giving the claims their broadest reasonable interpretation "a portion of an antibody" reads on a single amino acid. The Examiner further stated that the state of the art does not recognize the interaction of the CCR5 receptor with a single amino acid. The Examiner stated that, rather, chemokine receptors interact with a number of known ligands including RANTES, MEP-1-a and MIP-1-p (citing the specification

at page 11, lines 15-19). The Examiner stated that the level of predictability in the art would not permit one of ordinary skill to determine those portions of an antibody that would interact with the CCR5 receptor. The Examiner also stated that this results from the fact that whether a protein interacts with an antibody or other ligand is determined by distinct conformational properties that make the interaction highly specific. The Examiner asserted that the amount of direction provided by applicants' specification would not allow one of ordinary skill to overcome the lack of predictability in the binding properties of CCR5. The Examiner stated that this results from applicants' failure to show any working examples of CCR5 interacting with either an antibody or a portion of an antibody. The Examiner further stated that applicants' specification only demonstrates the interaction of CCR5 with a number of chemokine proteins. The Examiner also stated that one of ordinary skill would therefore have to perform significant experimentation in order to identify the broad range of antibodies, or portions of antibodies, that are capable of binding CCR5. The Examiner concluded that, based on the foregoing, applicants' specification would not enable one of ordinary skill to make and use applicants' invention without undue experimentation.

In response, applicants respectfully traverse this rejection. Without conceding the correctness of the Examiner's position, applicants note that claims 51-55, as amended, do not recite a "portion of an antibody." Accordingly, applicants respectfully submit that the Examiner's remarks regarding the recitation of a "portion of an antibody" are moot.

Regarding the Examiner's statement that applicants do not show any working examples of CCR5 interacting with an antibody, applicants note that, as stated in the specification at page 12, lines 12-13, antibodies against a chemokine receptor may easily

be generated by routine experiments. Applicants respectfully direct the Examiner's attention to the specification at, *inter alia*, page 22, lines 8-27 and page 33, line 1 to page 34, line 30, which discloses PCR primers and methods for cloning nucleotide sequences encoding chemokine receptors and for expressing such receptors in mammalian CD4+ cell systems. Applicants maintain that, based on the disclosures in the specification and given the high level of skill in this field, one skilled in the art would readily be able to make an antibody capable of binding to a chemokine receptor, including CCR5, on the surface of a CD4+ cell without undue experimentation.

Applicants note that independent claim 51, as amended, recites that an antibody capable of binding to a chemokine receptor on the surface of a CD4+ cell must also inhibit HIV-1 infection of such cell. Regarding this limitation, applicants respectfully direct the Examiner's attention to disclosures in the specification relating to the inhibition of HIV-1 infection of CD4+ cells as a result of inhibiting fusion of HIV-1 to such cells (see, *inter alia*, page 4, lines 8-13); the availability of the resonance energy transfer (RET) assay for easily identifying agents that inhibit fusion of HIV-1 to CD4+ cells (see, *inter alia*, page 17, line 33 to page 18, line 15); and the routine nature of this screening methodology (see, *inter alia*, page 22, lines 27-30). Applicants maintain that these disclosures fully enable amended claim 51.

In view of the remarks set forth above, applicants respectfully submit that disclosures in the specification as filed enable one skilled in the art to make the invention of claims 51-56, as amended, without undue experimentation. Applicants therefore request that the "enablement" rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

Written Description

The Examiner further rejected claims 51-56 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner also stated that in the present case, applicants' invention is directed to an antibody or portion of an antibody capable of biding to the CCR5 receptor. The Examiner further stated that, however, applicants' specification does not disclose any experimentation wherein a CCR5 antibody, or portion of a CCR5 antibody, was produced or used. The Examiner concluded that, accordingly, applicant has not shown possession of the claimed invention at the time the application was filed.

In response, applicants respectfully traverse this "written description" rejection. Without conceding the correctness of the Examiner's position, applicants note again that claims 51-55, as amended, do not recite a "portion of an antibody." Accordingly, applicants respectfully submit that the Examiner's remarks regarding this claim language are moot.

In response to the Examiner's statement that applicants' specification does not disclose any experimentation wherein a CCR5 antibody was produced or used, applicants hereby incorporate their remarks made above with regard to the "enablement" rejections under 35 U.S.C. §112, first paragraph. Applicants maintain that their description in the specification of an antibody capable of binding to a chemokine receptor, including CCR5, on the surface of a CD4+ cell is adequate to show possession of the claimed invention at the time the application

was filed. In this regard, applicants respectfully direct the Examiner's attention to the routine nature of methods for generating antibodies, which methods were available at the time of filing (see the specification at, *inter alia*, page 12, lines 12-13). Applicants also direct the Examiner's attention to methods disclosed in the specification for cloning nucleotide sequences encoding chemokine receptors and for expressing the receptors in mammalian CD4+ cell systems (see, *inter alia*, page 22, lines 8-27; page 33, line 1 to page 34, line 30); for screening agents using the RET assay for their ability to inhibit fusion of HIV-1 to CD4+ cells (see, *inter alia*, page 17, line 33 to page 18, line 15), thereby inhibiting HIV-1 infection of CD4+ cells (see, *inter alia*, page 4, lines 8-13). Applicants also note the routine nature of methods disclosed in the specification for testing antibodies for their ability to inhibit infection of susceptible cells by HIV-1 (see the specification at, *inter alia*, page 22, lines 27-30).

In view of the above-identified disclosures in the specification and the high level of skill in the art, applicants maintain that antibodies capable of binding to a chemokine receptor on the surface of a CD4+ cell and inhibiting HIV-1 infection of such cell need not have been experimentally produced. Applicants further maintain that these disclosures are adequate to show applicants' possession of the claimed invention at the time the specification was filed. Applicants therefore respectfully submit that the specification as filed satisfies the written description requirement of 35 U.S.C. §112, first paragraph, with regard to claims 51-56, as amended.

Rejections under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 51-56 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly

point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that claim 52 recites "[t]he antibody or portion of an antibody" in the first line of the claim, but that there is no antecedent basis for this limitation in the claim.

In response, applicants note that claim 52, as amended, depends from claim 51. Accordingly, the antecedent bases for limitations in claim 52, as amended, are present in claim 51.

The Examiner further stated that claims 51-52 are also indefinite in their recitation of "a portion of an antibody." The Examiner noted again that "a portion of an antibody" reads on a single amino acid. The Examiner stated that a single amino acid is incapable of recognizing specific epitopes within a chemokine receptor, and thus, it is unclear how "a portion of an antibody" is capable of binding the claimed chemokine receptors.

In response, and without conceding the correctness of the Examiner's position, applicants note that the phrase "a portion of an antibody" is not recited in any of the instant claims, as amended. Applicants respectfully submit, therefore, that this rejection is moot.

The Examiner also stated that claim 55 is further rejected under 35 U.S.C. 112, second paragraph for the recitation of a "PMBC" cell. The Examiner additionally stated that this acronym requires clarification within the claim before it can be recited.

In response, applicants note that claim 55, as amended, clarifies that the correct acronym is "PBMC" (i.e., not "PMBC") which is an abbreviation for peripheral blood mononuclear cell(s). Applicants note that the meaning of this abbreviation is disclosed in the specification at page 11, lines 27-29.

Conclusion

In view of the remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the claim rejections set forth in the May 5, 2004 Office Action, and earnestly solicit allowance of all claims pending in the subject application.